Remarks

Applicants have canceled claims 23-27 without prejudice to Applicants' rights to pursue their subject matter in the present application and in other applications. Applicants have amended claim 32 to recite a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a nonpeptide small molecule, wherein the composition is formulated to be compatible with an intended route of administration to a subject. Support for the amendment is found in the original application at least at pages 51 ("pharmaceutically acceptable carrier"; "suitable for administration to a subject"; "formulated to be compatible with its intended route of administration") and 66 ("nonpeptide small molecules").

Applicants have added new claims 35 and 36. Support for new claims 35 and 36 is found in the original application at least at pages 51-54.

Applicants submit that the amendments introduce no new matter into the application.

Upon entry of this paper, claims 32-36 will be pending and presented for examination.

35 U.S.C. § 112—new matter

The Office action rejected claims 23-27 as allegedly failing to comply with the written description requirement, noting the recitation of compositions having greater affinity for IGFBP-2 than for IGFBP-1, IGFBP-3, IGFBP-4, IGFBP-5, and IGFBP-6 and alleging that this recitation was unsupported by the original application. Applicants disagree.[1] Nevertheless, Applicants have canceled claims 23-27 to promote prosecution and respectfully request withdrawal of the rejection.

[1] See, for example, page 60 of the application: ("It has previously been demonstrated that the isoquinoline analogue NBI-31772 dissociates IGF-I from its binding protein complex"; "It is also known that NBI-31772 inhibits interaction of IGF-I with IGFBP-1 to 6; "The highest activity of the isoquinoline analogue NBI-31772 is toward IGFBP-2, compared to the other five IGFBPs")

35 U.S.C. § 112

The Office action rejected claims 23-27 as allegedly failing to comply with the enablement requirement. As noted previously, Applicants have canceled the rejected claims to promote prosecution and without acquiescing to the rejections. Applicants therefore request withdrawal of the rejection.

35 U.S.C. 102

Liu

The Office action rejected claims 23-27 and 32-34 under 35 U.S.C. § 102(b) as allegedly anticipated by Liu *et al.* (2001) J. Biol. Chem. 35:32419-32422 ("Liu"). Applicants disagree and respectfully request reconsideration and withdrawal of the rejection.

As amended, claims 32-34 (and new claims 35-36) relate to *pharmaceutical compositions* comprising a *pharmaceutically acceptable carrier* and a nonpeptide small molecule which dissociates a protein complex comprising an insulin-like growth factor (IGF) and an insulin-like growth factor binding protein (IGFBP), wherein the composition is *formulated to be compatible with an intended route of administration to a subject.*

Liu does not teach the claimed *pharmaceutical compositions.* Liu teaches NBI-31772 and its use in *in vitro* studies, one involving a mixture with a radioactive IGF-1 protein and one involving administration to mouse fibroblast cells being cultured in flasks in the presence of fetal bovine serum, culture medium, IGFBP-3 isolated from outdated human plasma, and IGF-1. Liu does not administer a composition to a subject. Liu provides no indication that any of its NBI-31772 compositions have been formulated to be compatible with administration to a subject (making no reference, for example, to sterility, purity of ingredients, *etc.*). Liu does not indicate that any of its NBI-31772 compositions would be pharmaceutically effective.[2]

[2] Liu does not take the position that NBI-31772 is even a candidate drug for any indication, although Liu does suggest that it could be used as a lead molecule: "NBI-31772 could serve as a valuable lead molecule for the design of drug candidates for treatment of diabetes or other IGF-responsive diseases" (p. 32422).

Liu therefore fails to disclose the claimed invention and cannot anticipate the claims under 35 U.S.C. § 102.

Applicants request reconsideration and withdrawal of the rejection.

Sakano

The Office action rejected claims 32-34 under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,428,781 ("Sakano"). Applicants request reconsideration and withdrawal of the rejection.

Although Applicants disagree with the rejection for all of the reasons set forth in Applicants' prior paper, to promote prosecution, Applicants have amended the claim to recite a pharmaceutical composition comprising a *nonpeptide* small molecule. Sakano does not teach a *nonpeptide* small molecule that dissociates a protein complex comprising an insulin-like growth factor and an insulin-like growth factor binding protein.

Applicants therefore request reconsideration and withdrawal of the rejection.

Conclusion

Upon entry of this paper, claims 32-36 will be pending and presented for examination. Applicants respectfully request the issuance of a notice of allowance.

Examiner Lu is invited to telephone the undersigned attorney to discuss any remaining issues.

Respectfully submitted,

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